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Original Research Article

Unveiling the Utility of Bronchoalveolar Lavage Cytology in Diagnosing Pulmonary Lesions at Tertiary Care Hospital

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Abstract:

Introduction: Bronchoalveolar Lavage (BAL) is a diagnostic procedure used to retrieve cells and various components from the bronchial and alveolar spaces for a range of investigative purposes. This minimally invasive day-care procedure serves a pivotal role in the diagnostic assessment of interstitial lung diseases, pulmonary infiltrates, and infectious conditions.

Aims and Objectives: (1). To evaluate the diagnostic accuracy of specimens acquired through bronchoalveolar lavage (BAL). (2). To explore their correlation with histopathological findings wherever available, both in cases of malignant and non-malignant lung lesion.

Material Methods : The retrospective and prospective observational study was conducted in cytology department over 19 months. For prospective analysis all BAL samples sent for cytological study were included while for retrospective analysis cytology reports of BAL samples were studied from records and included in the study. Cytology staining of smears was done and cytology evaluation was done by two cytologists. Histopathology correlation done on cases of positive for malignancy wherever available. Sensitivity, specificity diagnostic accuracy of BAL was obtained using SPSS software package version 22.

Results: In our study 61 cases of BAL for cytology were studied. Patients were presented with mainly complaints of cough (46%) and breathlessness (40%). Cases were broadly classified into 3 categories on cytology as 52% non- neoplastic, 41% were neoplastic and 7% were inadequate. After correlating cytology and histopathological diagnosis in 26 cases there was 1 false positive and 1 false negative case giving the sensitivity, specificity and accuracy of BAL cytology of 95%, 83.33% and 92.31% respectively with highly signficant p value indicate almost perfect agreement.

Conclusion: BAL cytopathology gives valuable adjunct to conventional diagnostic methods, offering insights into a spectrum of pulmonary diseases, including infections, inflammatory conditions, and neoplastic. In a tertiary care hospital, where complex and challenging cases are often encountered, the utility of BAL in cytology is indispensable. It aids in accurate diagnosis, guides appropriate treatment plans for patients.

Key words: Bronchoalveolar Lavage cytology, Diagnosis, Pulmonary lesions.

Introduction

Broncho-alveolar lavage (BAL) is a well-established investigating technique for diagnosing various pulmonary lesions. It involves the saline lavage of a segment of the lower respiratory tract. This procedure explores extensive regions of the alveolar compartment, offering a collection of both cellular and non-cellular components derived from the lower respiratory tract.[1,2] The material obtained through broncho-alveolar lavage (BAL) plays a crucial role in diagnosing infections and malignancies.(3)Initially designed as a therapeutic intervention for pulmonary conditions such as pulmonary alveolar proteinosis, cystic fibrosis, and intractable asthma, bronchoalveolar lavage (BAL) has not only gained acceptance but also steady popularity as a diagnostic tool for lung cancer.[4] Lung cancer ranks as the most commonly diagnosed major cancer globally and is the leading cause of cancer-related deaths worldwide.[5] Early diagnosis of lung cancer is crucial for successful treatment, ideally before the lesion progresses to a visible and palpable tumor stage.[5] While the preliminary

diagnosis of malignancy can be established through clinical and radiological assessments, the definitive diagnosis requires cytological or histopathological examinations of specimens obtained from the respiratory tract.[6] BAL clears alveolar spaces, reaching beyond obstructed sites, while bronchial wash technique samples areas inaccessible to brushes.[7] BAL, conducted with a video bronchoscope in a wedged position within the chosen bronchopulmonary segment, is a minimally invasive and well-tolerated procedure, ensuring safety.[5,8,9] Reliable investigations aid early-stage lung cancer diagnosis, facilitating effective treatment and improving patient survival. [10] The new World Health Organization (WHO) classification of lung tumors now incorporates cytological diagnosis alongside ancillary techniques, reflecting a pivotal evolution in diagnostic methodologies. [6] This study, conducted at a tertiary care hospital in Central India, aimed to assess the diagnostic value of bronchoalveolar lavage (BAL) in pulmonary diseases.[8]

Aims and Objectives:

- To evaluate the diagnostic accuracy of specimens acquired through bronchoalveolar lavage (BAL)
- To explore their correlation with histopathological findings wherever available, both in cases of malignant and non-malignant lung lesion

Material and Methods:

This is a retrospective and prospective observational study carried out in Department of Pathology, government medical college Nagpur over 19 months period that is July 2022 to December 2023. The samples were obtained by flexible fiber-optic bronchoscopy done by the pulmonologist. For prospective analysis all BAL samples sent for cytological study were included while for retrospective analysis cytology reports of BAL samples were studied from records and included in the study.

Inclusion criteria: All BAL samples of all age group that were received in our laboratory during the study period

Exclusion criteria: We excluded the smears having 1. Paucity of alveolar macrophages 2. Extensive epithelial cells. 3. Mucopurulent exudates. 4. Numerous red blood cells. 5. Degenerating changes

Patients having clinical symptoms indicative of respiratory disease and/or abnormalities in imaging studies underwent a thorough examination by clinicians. Those meeting specific criteria were chosen for bronchoscopy. Following the acquisition of informed consent, pulmonologists conducted the bronchoscopy procedure. The fluid samples obtained of bronchoalveolar lavage (BAL), were promptly sent to the laboratory without fixation. In instances where processing was anticipated to be delayed, the fluids were stored at 4°C for a period of 24 to 48 hours. After receiving sample processing was done. The sample was shaken to disperse the cells and poured into centrifuge tube then centrifuged for 10 minutes at 1500 RPM. Cell suspension was prepared. A minimum four slides were made. Two of these slides were fixed in 95% alcohol and stained using routine haematoxylin and eosin (H&E) and Papanicolaou (PAP) stains, followed by examination under a microscope. The remaining unfixed smears underwent staining with Leishman's stain and Ziehl–Neelsen (ZN) stain. The remaining material was kept for cell block. Cell block preparation was done by routine histopathology technique. Histopathological correlation with lung biopsy was done wherever available.

Statistical analysis: The data collected were tabulated and analysed by proportions and percentages, and sensitivity, specificity diagnostic accuracy of BAL was obtained using SPSS software package version 22.

Results

In this study, a total of 61 cases of BAL samples were received in our cytopathology department over period of July 23 to December 23. Out of total 25 cases were taken as retrospective cases and 36 cases were taken as prospective cases.

Table 1: Sex distribution of cases

Sex	No. of patients	Percentage (%)
Male	45	73
Female	16	27
Total	61	100

This study shows male preponderance comprising of (45) male and (16) females (Table no. 1)

Table 2: Age distribution of cases

Age range	No. of patients
0-20	3
21-40	3
41-60	42
61-80	13

Majority of patients were in the age range of 41 to 60 years with youngest being 12 years old and oldest of age 80 years old. (Table no. 2)

Table 3: Clinical symptoms

Clinical symptoms	No of patients	% of patient
Cough	58	46
Breathlessness	50	40
Fever	13	10
Haemoptosis	2	2
Weight loss	3	2

Patients were presented with mainly complaints of cough (46%) and breathlessness (40%) and rest were like fever, haemoptysis, weight loss. (Table no. 3)

Table 4: Radiological Findings

HRCT findings	No of patients	% of patient
Radiopaque Mass	23	50
Pleural effusion	10	22
Hilar lymphadenopathy	2	4
Ground glass opacity	1	2
No abnormality	10	22
Total	46	100

Radiographic finding were available in 46 cases which included radiopaque mass (50%), pleural fluid (22%), hilar lymphadenopathy (4%), ground glass opacity (2%) and no abnormalities seen in (22%). (Table no. 4)

Table 5: Cytological distribution of cases

Cytology Category	No of cases (%)
Neoplastic	25(41%)
Non- Neoplastic	32(52%)
Inadequate	4 (7%)

Cases were broadly classified into 3 categories on cytology as 52% non- neoplastic, 41% were neoplastic and 7% were inadequate. (Table no. 5)

Table 6: Cytopathological findings

Cytopathology findings	No. of cases
Inflammatory cells with reactive changes	29(47%)
Tuberculosis (AFB +ve)	02(3%)
Pulmonary alveolar proteinosis, (PAS +)	01(2%)
Suspicious of malignancy	23(38%)
Inadequate sample	04(7%)

BAL cytopathology smears were distributed as Inflammatory cells with reactive changes 29 (47%), Tuberculosis (AFB +ve) 02 (3%), Pulmonary alveolar proteinosis, (PAS +) 01 (2%), Suspicious of malignancy 25 (41 %) and Inadequate sample 04 (7%). (Table no. 6)

Table 7: Inflammatory BAL smears with their can be Differential diagnosis

Cellular	No. of cases	Differential Diagnosis
Lymphocytic	15(57%)	Hypersensitivity pneumonitis Tuberculosis Sarcoidosis
Neutrophilic	9(34%)	Idiopathic pulmonary fibrosis Bacterial pneumonia Asbestosis
Eosinophilic	01(4%)	Hyper eosinophilic syndrome Eosinophilic pneumonia Churg-Strauss syndrome
Mixed cellularity	06(5%)	Bronchiolitis obliterans organizing pneumonia (BOOP) Non specific interstitial pneumonia Inorganic dust disease

Inflammatory BAL smears were further categorized into according to predominant inflammatory cells (Table no. 7) with possible differentials diagnosis.

Table 8: Histopathological diagnosis of Lung biopsy

Histo-pathological diagnosis	**No of cases**	**Percentage %**
Adenocarcinoma	12	50
Squamous cell carcinoma	5	19
Undifferentiated malignancy	1	3
Malignant Small round cell tumour	1	3
Mesothelioma	1	3
Dysplasia	6	23
Total	26	100

26 cases which were given suspicious of malignancy on cytology on histopathology most were Adenocarcinoma 50%,(Fig 1,2) SCC (19%) (fig 3,4) (Table no.8)

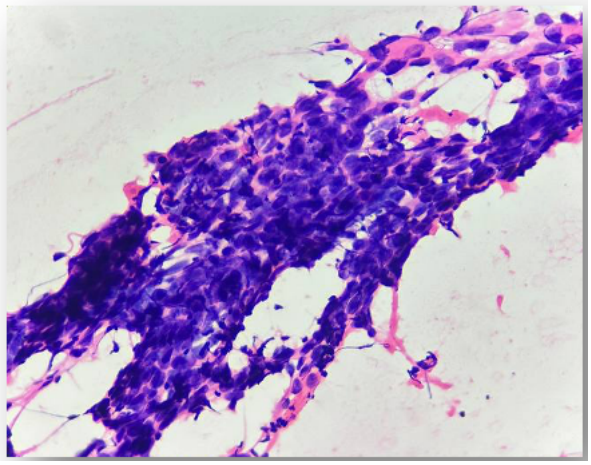

Figure 1: BAL Cytology Positive for malignancy (H&E 40X)

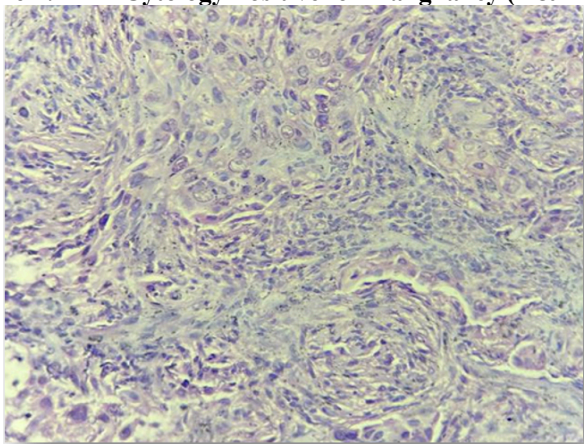

Figure 2: Lung Biopsy- Squamous Cell Carcinoma (H&E 40X)

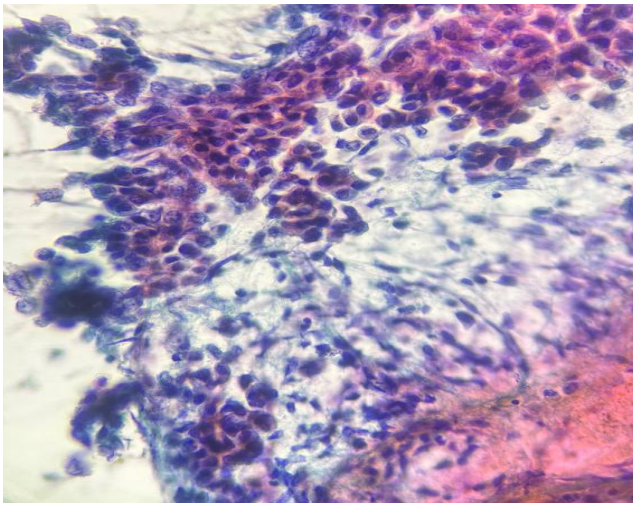

Figure 3: BAL Cytology Positive for malignancy (H&E 40X)

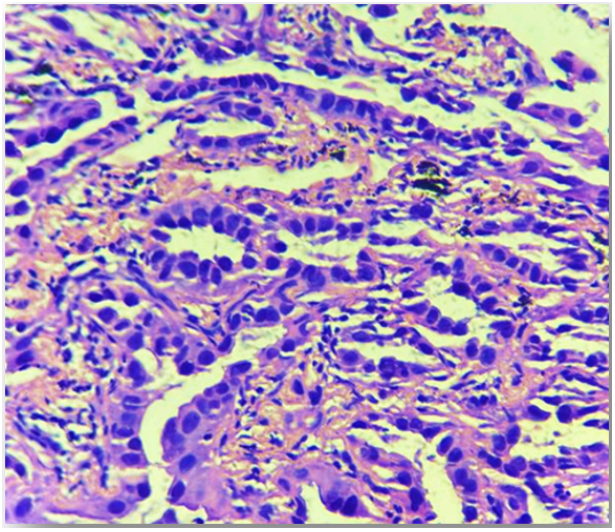

Figure 4: Lung Biopsy Adenocarcinoma (H&E 40X)

Table 9: Cytohistopathological correlation

Histo-pathology diagnosis	BAL Cytology Diagnosis				
	Adenocarcinoma	**scc**	**Suspicious on BAL**	**Reactive changes**	**Total**
Adenocarcinoma	02		10	-	12
Squamous cell carcinoma	-	02	03		05
Undifferentiated malignancy	-		01	-	01
Malignant Small round cell tumour	-		-	01	01
Mesothelioma	-		01	-	01
Dysplasia		+01	-	05	06
Total	02	03	15	06	**26**

After correlating correlating cytology and histopathological diagnosis in 26 cases there was 1 false positive and 1 false negative case. 1 case was false negative was reported on cytology as reactive atypia was diagnosed as malignant small round cell tumor on histopathology. 1 false positive case which on BAL cytology was reported as Squamous cell carcinoma was diagnosed on histopathology as dysplastic changes (table no. 9)

In our study, the sensitivity, specificity and accuracy of BAL cytology were 95%, 83.33% and 92.31% respectively with highly signficant p value indicate almost perfect agreement between both tests.

Table 10: Statistical Analysis

Statistical Parameter	Results
Sensitivity	95%
Specificity	83.33%
Positive predictive value	95%
Negative predictive value	83.33%
Diagnostic accuracy	92.31%
P value	<0.0001(significant)
Kappa value	0.78
Agreement	92.31%

Discussion

BAL is one of the important preliminary diagnostic tools which is preferred over invasive techniques like needle biopsies and thoracoscopy. Cytological assessment of specimens of respiratory tract is one of the important initial diagnostic techniques carried out in a patient with suspected lung lesion.[10] Moreover some malignancies of lung mimic infectious or inflammatory conditions posing major diagnostic problem. In such a clinical setting, BAL plays a relevant role in diagnosing or ruling out malignant lesions . The present study was done to compare and evaluate the efficacy of bronchial cytology with histopathology and the utility of bronchial cytology in diagnosis in patients where biopsy is contraindicated or biopsy site is not reachable.[10]

In our study, Lung malignancy showed male preponderance with male to female ratio 2.81 which is in concordance with the study done by Agarwal et al.[4] and Bhat N et al.[5] This may be due high incidence of smoking in males in India. Cough and breathlessness were found to be the most common presenting complaints and mass and pleural effusion were the most common radiographic findings in malignant cases of our study and the results which were very much lower compared with Sareen R et al.[10] In our study out of 61 cases BAL fluids analysed, 25 were categorised as neoplastic, 32 were non neoplastic, and 4 were inadequate. On comparing with biopsy we found 23 were correctly typed as malignant.

1 case was false negative which was given on cytology as reactive atypia was came out malignant small round cell tumor on histopathology. This may be due to non-representative material and sample retrieved might be less in amount and thus may have lesser cytological material than expected on cytology. This is in concordance with study done by Anandhi et al.[11] Malignant lesion may also be completely missed due to excess obscuring elements such as inflammatory cells or RBC's or due to non representative material on cytology.

1 false positive case which on BAL cytology was given Squamous cell carcinoma was given on histopathology as dysplastic changes. This can be due to misinterpretation of reactive cellular changes as features of malignancy. This is in concordance with Anandhi et al.[11]

In our study Adenocarcinoma (50%)was the commonest type of carcinoma of lung followed by squamous cell carcinoma (19 %) of lung which is comparable with study done by Agarwal, et al.[4] and M. Pavani et al.[6]

Table 11: Comparison with other similar studies

Study	No. of cases	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy	p value
Present study	61	95%	97.30%	95%	83.33%	93.54%	<0.0001
Sareen et al (2016) [10]	504	72.69%	100%	100%	76.95%	83.67%	-
Tayal S et al (2018) [1]	48	47.83%	100%	100%	37%	75%	-
George et al (2020) [12]	70	51%	100%	100%	43.18%	64.86%	-
Kedige et al(2023)[13]	12	100%	88.85%	75%	100%	91.6%	-

In our study, the sensitivity, specificity and accuracy of BAL cytology were 95%, 83.33% and 92.31% respectively which is comparable with other similar studies.(Table no.11)

There are some limitations of BAL while diagnosing pulmonarly lesions like the use of saline in BAL may dilute cell concentrations, impacting the sensitivity of cytological analysis. Reactive cellular changes may sometimes be misinterpreted as malignant lesions. Malignant lesion may be completely missed due to excess obscuring elements such as inflammatory cells or RBC. Accurate tumor subtyping may not always be possible on cytology specimens due to a lack of architectural patterns or low cellularity.

Neverthless the p value is highly significant in our study authenticating the importance of this non-invasive procedure. By doing proper BAL sampling,

screening and strictly adhering to adequacy criteria can minimize false negative and false positive cases in the study. Early and accurate diagnosis can contribute to improved patient outcomes, reducing the need for extended and costly treatments or hospitalizations. Ancillary techniques like immunocytochemistry, FISH, molecular testing can be performed on BAL samples.

Conclusion:

BAL cytopathology gives valuable adjunct to conventional diagnostic methods, offering insights into a spectrum of pulmonary diseases, including infections, inflammatory conditions, and neoplastic. In a tertiary care hospital, where complex and challenging cases are often encountered, the utility of BAL in cytology is indispensable. It aids in accurate diagnosis, guides appropriate treatment plans for patients.

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